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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/592,919	07/31/2007	Michael T. Migawa	CORE0037USA	2825

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McDermott Will & Emery LLP
600 13th Street, NW
Washington, DC 20005-3096

EXAMINER

BOWMAN, AMY HUDSON

ART UNIT	PAPER NUMBER
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1635

NOTIFICATION DATE	DELIVERY MODE
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10/21/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mweipdocket@mwe.com
SIP_Docket@mwe.com

Office Action Summary	Application No. 10/592,919	Applicant(s) MIGAWA ET AL.	
	Examiner AMY BOWMAN	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-32 is/are pending in the application.
- 4a) Of the above claim(s) 10, 14-16, 25 and 29-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-13, 19-24, 26-28, and 32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election without traverse of modified nucleotide, more specifically, modified base nucleotide, more specifically tetrafluoroindolyl, in the reply filed on 8/17/10 is acknowledged.

Claims 10, 14-16, 25, and 29-31, as well as the subject matter of the claims that is not directed to the elected invention, is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/17/10.

It is noted that applicant set forth that claim 24 does not read on the elected invention, which appears to be in error.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11-13, 17, 19-24, 26-28, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification does not describe the instantly claimed genus of transition moieties in a manner that would allow the skilled artisan to envision which moieties would in fact modulate the transmission of the conformation of the second region to the first region. The specification does not set forth any structural criteria to allow one to envision the genus of molecules that would in fact act via the claimed mechanism.

Furthermore, the specification does not set forth any structural criteria for modified bases to allow one to envision the genus of modified bases that do not form hydrogen bonds with the target RNA but optionally stack with adjacent bases.

With regards specifically to tetrafluoroindolyl, the instant specification does not describe the modification in a manner to demonstrate that it in fact acts via the mechanism of claim 11 or that two or more of such modifications between the claimed region would in fact transition the second region to the conformation of the second region.

For purposes of the instant search and corresponding examination, any modified nucleotide meets the instant limitation of the transition moiety and any of the bases set forth in claim 12 would necessarily act as claimed in claim 11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 17, 19-22, and 32 are rejected under 35 U.S.C. 102(a) or (e) as being anticipated by Krotz et al. (US 2003/0096770 A1).

The reference is of record and cited on the PTO-892 mailed on 2/18/10.

Krotz et al. teach a method of modulating the expression of a target RNA comprising administering an antisense oligonucleotide specific for the target. Krotz et al. teach an oligonucleotide that has a first region of nucleotides of one conformation, which comprises deoxynucleotides, and a second region that is 5' to the first region that comprises 2'-O-methoxyethyl groups. Additionally, the oligo comprises phosphorothioate linkages. There is a transitional moiety between the 2'-O-methoxyethyl and deoxynucleotides that incorporates a 5-methylcytosine (see ISIS-9606, page 8, for example). Additionally, the oligonucleotide has a third region of the same type as the second region that again is separated from a deoxynucleotide by a 5-methylcytosine.

Krotz et al. teach "chimeras" may be "gapmers," i.e., oligonucleotides in which a central portion (the "gap") of the oligonucleotide serves as a substrate for, e.g., RNase H, and the 5' and 3' portions (the "wings") are modified in such a fashion so as to have greater affinity for, or stability when duplexed with, the target RNA molecule but are

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unable to support nuclease activity (e.g., 2'-fluoro- or 2'-methoxyethoxy-substituted).

Krotz et al. teaches that the compounds are administered to humans and human cells.

Therefore, the instant claims are anticipated by Krotz et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11, 12, 17, 19-24, 26, 27, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krotz et al. (US 2003/0096770 A1).

Krotz et al. teach a method of modulating the expression of a target RNA comprising administering an antisense oligonucleotide specific for the target. Krotz et al. teach an oligonucleotide that has a first region of nucleotides of one conformation, which comprises deoxynucleotides, and a second region that is 5' to the first region that comprises 2'-O-methoxyethyl groups. Additionally, the oligo comprises phosphorothioate linkages. There is a transitional moiety between the 2'-O-methoxyethyl and deoxynucleotides that incorporates a 5-methylcytosine (see ISIS-9606, page 8, for example). Additionally, the oligonucleotide has a third region of the same type as the second region that again is separated from a deoxynucleotide by a 5-methylcytosine.

Krotz et al. teach "chimeras" may be "gapmers," i.e., oligonucleotides in which a central portion (the "gap") of the oligonucleotide serves as a substrate for, e.g., RNase H, and the 5' and 3' portions (the "wings") are modified in such a fashion so as to have greater affinity for, or stability when duplexed with, the target RNA molecule but are unable to support nuclease activity (e.g., 2'-fluoro- or 2'-methoxyethoxy-substituted).

Krotz et al. teaches that the compounds are administered to humans and human cells.

Additionally, Krotz et al. teach fluorinated oligonucleotides are preferred.

It would have been obvious to incorporate fluorinated nucleotides into the oligonucleotide of Krotz et al. set forth above since Krotz et al. teach each of the claimed modifications as preferred modifications to increase the binding affinity and enhance the overall activity of the oligonucleotide.

The specific oligonucleotide set forth above incorporates a 5-methylcytosine between each of the regions. It would have been obvious to incorporate 2 of such modifications as a matter of design choice and would certainly be within the realm of routine optimization of the molecule.

One would have a reasonable expectation of success in combining the modifications and resulting in active molecules given that Krotz et al. teach that each of the modifications enhance the activity of antisense oligonucleotides.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMY BOWMAN whose telephone number is (571)272-0755. The examiner can normally be reached on Monday-Thursday 6:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AMY BOWMAN
Primary Examiner
Art Unit 1635

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Primary Examiner, Art Unit 1635